Cutaneous Sarcoidosis

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KEYWORDS

• Cutaneous sarcoidosis • Granulomas • Noncaseating • Lupus pernio • Erythema nodosum
• Löfgren syndrome

KEY POINTS

- Skin is the second most common organ affected after the pulmonary system.
- Cutaneous sarcoidosis can be the presenting sign of systemic sarcoidosis, and work-up is indicated in all patients with cutaneous manifestations. Certain presentations can provide clues to prognosis and underlying systemic involvement.
- The skin is readily accessible for evaluation and biopsy. Biopsy of cutaneous disease is helpful and may be essential for diagnosis of systemic sarcoidosis; it can sometimes obviate more invasive testing.
- Health-related quality of life measures and objective assessment tools can help standardize evaluation.
- Treatment of cutaneous sarcoidosis should follow a therapeutic ladder with potential treatments based on additional organ involvement and extent of cutaneous disease with weighing of potential risks of therapy.

INTRODUCTION

Sarcoidosis is a multisystem, noncaseating granulomatous disorder of unknown cause with skin as the second most common organ affected, occurring in 25% to 30% of cases reported.[1–8] Cutaneous sarcoidosis may be the presenting sign of systemic disease and a high clinical index of suspicion is critical because there can be protean manifestations.[9,10] Sarcoidosis may affect patients of all races and at any age, although the clinical presentation may vary by ethnic background. African Americans are more often affected by chronic skin sarcoidosis compared with white people. Sarcoidosis is more common in women than in men, with African American women having the highest rates of sarcoidosis in the United States, including the highest rates of chronic cutaneous sarcoidosis. There is also a higher incidence of erythema nodosum in women.[2] Lesions can range from minimal skin involvement to extensive disease that results in significant morbidity and dramatic impact on quality of life. By strict definition, a diagnosis of sarcoidosis can only be rendered when there is more than 1 organ involved, and requires the presence of granulomatous inflammation in multiple systems.[11] If cutaneous involvement only is present, then a diagnosis of sarcoidlike granulomatous disease of unknown significance may be more precise, although some clinicians describe it as isolated cutaneous sarcoidosis; this is an area of active debate.[12]

SKIN PATHOPHYSIOLOGY

The exact inciting cause of sarcoidosis remains unknown. Sarcoidal inflammation is caused by a complex interplay of multiple factors, including genetics; environmental and/or infectious antigens;

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and the immune system, involving Th1 predominant response with interferon-gamma and tumor necrosis factor (TNF) playing an important role, and with emerging evidence suggesting a role of Th17 inflammation and interplay with the innate immune system.[13,14] Although sarcoidosis can affect any site on the skin, including the mucosa, cutaneous sarcoidosis preferentially occurs in sites of prior injury, such as scars, as well as in tattoos. Patients with sarcoidosis and tattoos may have none, some, or all of their tattoos affected, and cutaneous sarcoidosis can affect multiple tattoo pigments. Notably, polarizable material may be seen in approximately 25% (ranges of 20%–78% have been reported) of skin biopsies of sarcoidosis, suggesting that in some patients foreign material serves as a nidus for granuloma formation.[15–20] Although not the sole cause of disease, foreign bodies, scars, and trauma may affect the distribution of skin lesions in patients with sarcoidosis.

CLINICAL PRESENTATION

Cutaneous sarcoidosis can present in various ways and is often considered an imitator of other skin diseases. Skin disease is often present at disease onset and activity correlates with systemic inflammation in many cases, although cutaneous sarcoidal inflammation may be discordant with internal involvement as well. Skin manifestations can be divided into specific lesions and nonspecific lesions: specific manifestations refer to the presence of noncaseating granulomas observed within skin biopsies, and nonspecific lesions are considered reactive to systemic sarcoidosis but do not have granulomas on biopsy (this refers primarily to erythema nodosum).

Although specific lesions of cutaneous sarcoidosis are widely variable, certain manifestations are observed more frequently than others. In addition, some morphologies may be associated with better or worse prognosis, and in some cases may be a clue as to particular patterns of internal organ involvement.

Common Morphologies

Macules/papules

One of the commonest morphologies affecting the skin includes lesions smaller than a centimeter, either macules (flat lesions) or papules (raised lesions).[21] These lesions can range in color and may be red/violaceous, skin colored to brown, and even hypopigmented (Fig. 1A). Often, there are numerous macules or papules that can be disseminated or concentrated in certain areas, such as the central face, extremities, and areas of trauma.[21–23] Papular sarcoidosis shows a predilection for knees or sites of repetitive trauma in some patients (Fig. 1B).[22] Macules and papules have been described as more common in acute forms of sarcoidosis and may be seen in association with erythema nodosum; they may also occur in patients with chronic disease.[1,24] Overall, these lesions portend a good prognosis with on average less than 2 years of active systemic sarcoidosis, and often self-resolve without scarring.[24]

Plaque

As skin lesions become larger than 1 cm, they are defined as plaque sarcoidosis. In addition to papular sarcoidosis, this is one of the commonest lesions and can be found on face, back, buttocks, and often on the extensor surfaces of arms (Fig. 2).[2,8,24,25] Compared with macules/papules, plaque sarcoidosis is less often associated with acute presentation of disease, does not occur in conjunction with erythema nodosum as frequently, and often predicts a more chronic course with a higher likelihood of recurrence.[2,8,24] In addition, systemic symptoms also seem to be more chronic, lasting longer than 2 years in most cases, and individuals can have persistent symptoms, including bilateral hilar lymphadenopathy, splenomegaly, pulmonary fibrosis, and uveitis, although these associations are based on small studies (Fig. 3).[1,7,9,10,24,26,27] Compared with macules/papules, plaque sarcoidosis is more likely to leave dyspigmentation and scarring.

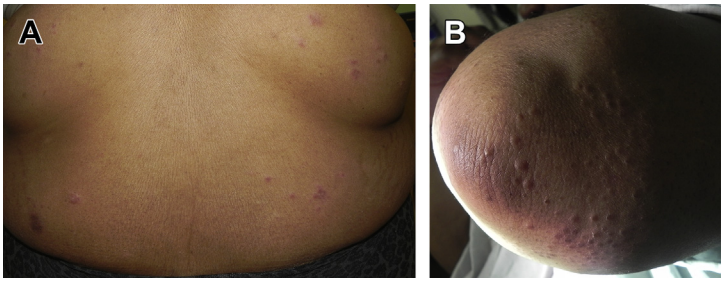

Fig. 1. Papular sarcoidosis. Scattered violaceous papules (<1 cm) on the back (*A*) and erythematous papules on the elbow (*B*), most likely reflecting a site of trauma.